EDITORIAL

Aryl Hydrocarbon Receptor (AhR) as a Potential Therapeutic Target in Oral Diseases

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World Journal of Dentistry (2023): 10.5005/jp-journals-10015-2144

Dear Editor,

The aryl hydrocarbon receptor (AhR) is a highly evolutionarily conserved transcription factor and has been reported to have a crucial role in inflammatory modulation. Its expression is variable and is predominantly expressed in epithelial barriers. AhR is activated by molecules of low molecular weight of diverse chemical characteristics, both xenobiotic (exogenous) and endogenous, and can create cell or ligand-specified alterations in expression, and cell functions.[1] It is a basic helix-loop-helix type of transcription factor crucial for adaptive responses against xenobiotics. A vast number of studies indicated that as a transcription factor AhR has potential functions in metabolic regulation, immune and nervous systems, the interaction of host microbiota, maintenance of barrier organs, and development of cancer.[2]

Oral diseases are important of the most prevalent diseases worldwide seriously affecting the health and economy, moreover adversely diminishing the quality of life of the affected individual. Globally, the most predominant and consequential oral diseases are dental caries (tooth decay), loss of a tooth, periodontal diseases, and cancers of the oral cavity and lips. Children from poverty, socially marginalized crowd, and elderly people are greatly affected by oral diseases and have less access to dental care.[3] Quite a lot of studies have established the role of AhR in immune responses, depressive disorders, inflammation, cancers, inflammatory bowel disease, multiple sclerosis, etc. However recently a couple of studies have demonstrated the potential involvement of AhR in oral disease.[4]

A study by Martins et al. revealed the highly elevated expression of AhR in peri-implantitis patients' soft tissues compared to healthy tissues. As peri-implantitis is explained as an inflammatory condition caused by bacteria, and the alterations in expression and activation of AhR might be linked to the condition of dysbiosis. Microorganisms can produce activators of AhR, and accordingly, the AhR-dependant host response modulates the microbiota *via* quorum-sensing activity.[1] Another study in oral squamous cell carcinoma (OSCC) samples established significantly elevated expression of AhR in comparison with the normal oral mucosa, indicating the role of AhR in the initiation, promotion, and progression of OSCC. Several studies revealed the fact that the AhR-dependent pathway is essential for the initiation of a tumor by polycyclic aromatic hydrocarbons (PAHs), and the same is crucial in tumor promotion by enhancing the release from contact inhibition and also by blocking apoptosis.[1,5] Another study identified that AhR represses antitumor immune responses in OSCC by influencing directly malignant cells or indirectly in the tumor microenvironment. This study highlighted AhR as a crucial repressor of immunity against tumors and reinforce the hypothesis that focusing on AhR is an efficient route for concurrent inactivation of various immune checkpoints specifically tumors that have been checked for AhR activity and expression.[6]

A study by Zeng et al. investigated the impact of AhR in the pathogenesis of human fibrous epulis. Epulis is the hyperplasia of the gum mainly situated in the area of the gingival papilla and it displays a tumor-like appearance. It derives from the connective tissue of the gingiva and periodontal ligament. The study revealed the elevated expression of both mRNA and protein levels of AhR in fibrous epulis tissues. The over-expressed AhR in fibrous epulis tissue might have been involved in the pathogenesis of epulis by mediating the expression of proinflammatory and apoptosis-related factors. Hence AhR can be a potent target for the treatment of fibrous epulis.[2]

Recently oral epithelial cells pointed out as crucial inflammatory regulators related to periodontitis. Researchers suggest that 1,25-dihydroxyvitamin D3 inhibited LPS-induced overexpression of IL-6 *via* AhR/NF-κB signaling in human oral epithelial cells in an in vitro model.[7] They also confirmed the protective effect of 1,25-dihydroxyvitamin D3 against periodontitis by modulating the AhR/NF-κB/NLRP3 pathway in a mouse model.[8] Both studies demonstrated the suppression of AhR in periodontitis. Huang et al. also investigated the downregulation of AhR in inflammation in experimental periodontitis.[9]

The above cited scientific reports highlighted the potential role of AhR in various oral diseases through multiple pathways. Hence targeting AhR can be a potential therapeutic option for oral diseases like oral cancer, periodontitis, peri-implantitis, and epulis. As it is a receptor a potent ligand that can modulate the action of AhR may be a potent therapeutic intervention against oral diseases.

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How to cite this article: Sankaran K, Priya VV. Aryl Hydrocarbon Receptor (AhR) as a Potential Therapeutic Target in Oral Diseases. World J Dent 2023;14(1):1–2.

Source of support: Nil

Conflict of interest: None

References

1. Martins LRL, Grzech-Leśniak K, Castro Dos Santos N, et al. Transcription factor AhR, cytokines IL-6 and IL-22 in subjects with and without peri-implantitis: a case control-study. Int J Environ Res Public Health 2022;19(12):7434. DOI: 10.3390/ijerph19127434
2. Zeng X, Xia S, Yan X, et al. High expression of aryl hydrocarbon receptor (AhR) plays an important role in the formation of fibrous epulis. Oral Dis 2021. DOI: 10.1111/odi.13940
3. Yactayo-Alburquerque MT, Alen-Méndez ML, Azañedo D, et al. Impact of oral diseases on oral health-related quality of life: a systematic review of studies conducted in Latin America and the Caribbean. PLoS One 2021;16(6):e0252578. DOI: 10.1371/journal.pone.0252578
4. Neavin DR, Liu D, Ray B, et al. The role of the aryl hydrocarbon receptor (AHR) in Immune and inflammatory diseases. Int J Mol Sci 2018;19(12):3851. DOI: 10.3390/ijms19123851
5. Mony V, Nirmal RM, Parvathi V, et al. Evaluation of aryl hydrocarbon receptor expression in oral squamous cell carcinoma and normal oral mucosa using western blot. J Oral Maxillofac Pathol 2021;25(1):68–73. DOI: 10.4103/jomfp.JOMFP_287_20
6. Kenison JE, Wang Z, Yang K, et al. The aryl hydrocarbon receptor suppresses immunity to oral squamous cell carcinoma through immune checkpoint regulation. Proc Natl Acad Sci U S A 2021;118(19):e2012692118. DOI: 10.1073/pnas.2012692118
7. Li H, Li W, Wang Q. 1,25-dihydroxyvitamin D_3 suppresses lipopolysaccharide-induced interleukin-6 production through aryl hydrocarbon receptor/nuclear factor-κB signaling in oral epithelial cells. BMC Oral Health 2019;19(1):236. DOI: 10.1186/s12903-019-0935-x
8. Li H, Zhong X, Li W, et al. Effects of 1,25-dihydroxyvitamin D3 on experimental periodontitis and AhR/NF-κB/NLRP3 inflammasome pathway in a mouse model. J Appl Oral Sci 2019;27:e20180713. DOI: 10.1590/1678-7757-2018-0713. Available from: https://www.scielo.br/j/jaos/a/KQyJKW8TgthPMKVcgRyYs5s/?lang=en&format=pdf
9. Huang J, Cai X, Ou Y, et al. Protective roles of FICZ and aryl hydrocarbon receptor axis on alveolar bone loss and inflammation in experimental periodontitis. J Clin Periodontol 2019;46(9):882–893. DOI: 10.1111/jcpe.13166